ORAL ARGUMENT NOT YET SCHEDULED

No. 24-5235

IN THE

United States Court of Appeals for the District of Columbia Circuit

NOVARTIS PHARMACEUTICALS CORPORATION,
Plaintiff-Appellant,

v.

XAVIER BECERRA, SECRETARY OF HEALTH AND HUMAN SERVICES, et al.,
Defendants-Appellees,

and

MSN PHARMACEUTICALS INC., et al.,
Intervenor-Appellees.

On Appeal from the United States District Court
for the District of Columbia, No. 24-cv-02234
(Before Dabney L. Friedrich, J.)

EMERGENCY MOTION FOR ADMINISTRATIVE STAY AND STAY PENDING APPEAL OF FDA'S APPROVAL OF THE MSN PRODUCT

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January 12, 2025

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CERTIFICATE AS TO PARTIES, RULINGS, AND RELATED CASES

Pursuant to Circuit Rule 28(a)(1), Novartis Pharmaceuticals Corporation certifies that:

A. PARTIES

1. The following are parties in this Court:

   a. Plaintiff-Appellant: Novartis Pharmaceuticals Corporation.

   b. Defendant-Appellees: Xavier Becerra, in his official capacity as Secretary of the United States Department of Health and Human Services, and Robert M. Califf, in his official capacity as the Commissioner of the Food and Drug Administration.

   c. Intervenor-Defendants: MSN Pharmaceuticals Inc. and MSN Laboratories Private Ltd.

2. For purposes of Federal Rule of Appellate Procedure 26.1 and Circuit Rule 26.1, Novartis Pharmaceuticals Corporation certifies that Novartis Finance Corporation is its direct parent corporation, and that Novartis Pharmaceuticals Corporation is an indirect, wholly-owned subsidiary of Novartis AG.

B. RULINGS UNDER REVIEW

Plaintiff-Appellant appeals an order and memorandum opinion issued on October 13, 2024, by District Judge Dabney L. Friedrich, ECF Nos. 64, 65. This

order and opinion granted Defendants-Appellees' Cross Motions for Summary Judgment (ECF Nos. 43, 46) and denied Plaintiff-Appellant's Motion for Summary Judgment (ECF No. 38).

C. RELATED CASES

The appeal docketed as *Novartis Pharmaceuticals Corporation v. Becerra* (D.C. Cir. 24-05186) was a related case under Circuit Rule 28(a)(1)(C). This Court dismissed the appeal as moot on October 31, 2024.

/s/ Catherine E. Stetson
Catherine E. Stetson

Counsel for Novartis Pharmaceuticals Corporation

GLOSSARY

ANDA	Abbreviated New Drug Application
FDA	Food and Drug Administration
FDCA	Food, Drug, and Cosmetic Act
LVEF	Left Ventricular Ejection Fraction
MSN	MSN Pharmaceuticals
NDA	New Drug Application

INTRODUCTION

FDA approved a purported generic drug that references Novartis's best-selling drug product ENTRESTO® (sacubitril/valsartan). In doing so, FDA violated the agency's plain statutory and regulatory mandate that a generic drug be the "same" as its reference listed drug. The District Court, however, rejected those arguments and granted judgment for FDA and the intervenor generic manufacturer.

Merits briefing in this appeal is underway. The need for this stay arose late in the afternoon on January 10, when the U.S. Court of Appeals for the Federal Circuit lifted an administrative injunction precluding Intervenor MSN from launching its purported generic—despite ruling in Novartis's favor on the merits of its patent appeal earlier in the day. Later that day, the trial court overseeing the patent litigation restrained MSN from launching its product through January 15, 2025. At that point, the patent will expire. MSN has forecast its intention to launch its unlawful generic product at the earliest opportunity.

The impact of the MSN launch will be felt *immediately*. Once MSN's product hits the shelves, it will be automatically substituted for ENTRESTO at pharmacies and quickly take over a vast percentage of ENTRESTO's sales, insurers will move ENTRESTO to a lower formulary tier, and it will be virtually impossible for Novartis to recover this important market for its best-selling product. And because patients and physicians are frequently unaware when a generic product has been

substituted for a brand-name product, patient injuries caused by the carved-out labeling challenged in this APA lawsuit will jeopardize Novartis's relationships with physicians, patients, insurers, and distributors.

Novartis requests an administrative stay by 5 PM on January 13, 2025, and a stay pending appeal by 5 PM on January 15, 2025.

BACKGROUND

A. Statutory and Regulatory Background

Drug Approval Process

The Federal Food, Drug, and Cosmetic Act (FDCA) provides the statutory framework for FDA's regulatory oversight of drug products. To gain approval to market a new brand-name drug, a manufacturer submits a New Drug Application (NDA), demonstrating with scientific studies that the drug is safe and effective. 21 U.S.C. § 355(b)(1). Generic drugs are approved through an Abbreviated New Drug Application (ANDA). 21 U.S.C. § 355(j). An ANDA need not independently demonstrate safety or effectiveness; it need only establish that the generic product is "the same as" a reference listed drug already known to be safe and effective. *See* 21 U.S.C. § 355(j)(2).

Same-Labeling Requirement

The FDCA generally requires an ANDA applicant to demonstrate that its proposed labeling is the same as the labeling for the reference listed drug. 21 U.S.C.

§ 355(j)(2)(A). FDA has issued regulations addressing the limited exceptions to the same-labeling requirement. 54 Fed. Reg. 28,872, 28,884 (July 10, 1989) (noting that the exceptions to the same-labeling are "limited."). FDA regulations provide that the generic drug product may reflect labeling differences to address marketing exclusivity or patent rights, so long as "such differences do not render the proposed drug product less safe or effective than the listed drug for all remaining, non-protected conditions of use." 21 C.F.R. §§ 314.127(a)(7), 314.94(a)(8)(iv).

The agency also directed that labeling differences designed to avoid patent protection or regulatory exclusivity must take the form of an omission of language. *Id.* § 314.94(a)(8)(iv).

B. Novartis's ENTRESTO

ENTRESTO was approved by FDA in July 2015. ENTRESTO is currently approved to reduce the risk of cardiovascular death and hospitalization for heart failure in adult patients with chronic heart failure. It also has an approved pediatric indication. AR 1470.

Heart failure patients are sometimes classified by their left ventricular ejection fraction (LVEF). Ejection fraction is a measurement, expressed as a percentage, of how much blood the heart's left ventricle pumps out with each contraction.

ENTRESTO's initial indication, in patients with chronic heart failure and reduced ejection fraction (HFrEF), was based on the results of a clinical trial that

enrolled patients with heart failure with *reduced* ejection fraction of *less than* or equal to 40%. AR 241–243.

The PARAGON-HF Trial

In February 2021, FDA approved a supplement to ENTRESTO's NDA. AR 1466–68. The supplement was premised on the results of a second clinical trial, known as the PARAGON-HF trial, which enrolled patients with chronic heart failure and LVEF *greater than* or equal to 45%. AR 3964–66. Based on the combined results of both trials, the ENTRESTO indication was expanded to include not only chronic heart failure patients with reduced ejection fraction, but also those with LVEF greater than 40%, including those with preserved ejection fraction (that is, the ejection fraction is 50% or higher at diagnosis) (HFpEF). AR 1470, AR 1491. ENTRESTO is now approved to treat *all* patients with chronic heart failure, whether classified as having reduced ejection fraction or not. AR 1470, 3980.

This approach reflects the modern understanding of heart failure, because the medical community has transitioned away from using LVEF as a strict criterion for classifying heart failure. AR 3821–47.

The TITRATION Study

ENTRESTO's labeling describes a modified dosing regimen for patients not taking an angiotensin-converting enzyme (ACE) inhibitor or an angiotensin II receptor blocker (ARB)—two drugs that increase blood flow—or who were

previously taking low doses of these agents before starting ENTRESTO.[1] AR 1471. The labeling directs physicians and such patients to initiate treatment with a reduced dose of ENTRESTO and then to up-titrate to the target dose more slowly than is used for other patients. AR 1471.

This modified dosing regimen is derived from a clinical study known as the TITRATION study, which demonstrated that the dosing regimen in Section 2.6 of the ENTRESTO labeling resulted in fewer clinically relevant adverse events for this patient group and allowed them to reach the efficacious target dose. AR 3982–84; AR 3949.

Because of Novartis's patent protection, Declaration of Travis Roop (Roop Decl.) ¶ 4, FDA is prohibited from approving generic labeling that references the patented uses until the expiration of the relevant patents if a generic applicant does not challenge each patent, or challenges each patent but does not prevail. 21 U.S.C. § 355(j)(5)(B)(ii)-(iii).

C. The Same Active Ingredient Citizen Petition

In April 2019, Novartis submitted a citizen petition to FDA explaining that any generic version of ENTRESTO must have the same active ingredients in the same chemical form as ENTRESTO. AR 2812–38. In that petition, Novartis argued that the two active ingredients in ENTRESTO are in a single chemical structure and

[1] These patients are called "ACE-inhibitor or ARB naive patients."

that this chemical structure must serve as the basis for establishing active ingredient sameness for any proposed generics. AR 2817–31.

D. The Labeling Carve-Out Citizen Petition

In September 2022, Novartis submitted a citizen petition to FDA explaining that it would be unlawful for FDA to revise the approved indication for purported generic versions of ENTRESTO by rewriting the indication to cover only patients with *reduced* ejection fraction. AR 3959–3990. Novartis also explained that FDA was prohibited from carving the modified dosing regimen out from generic labeling because to do so would be to render the purported generic product less safe and effective than ENTRESTO for the remaining conditions of use. AR 3982.

E. FDA's Approval of the MSN Product and Novartis's Lawsuit

On May 28, 2024, FDA denied Novartis's Same Active Ingredient Citizen Petition. AR 2783–2808. Specifically, the agency rejected Novartis's argument that the "same active ingredient" analysis should be based on the salt structure present in the finished dosage form of Entresto—that is, sacubitril and valsartan in ionic coordination with sodium with 1:1:3 stoichiometry.

On July 24, 2024, FDA denied Novartis's Labeling Carve-Out Citizen Petition. AR 3910–54. The next day, FDA updated the Orange Book to reflect its approval of an ANDA submitted by MSN identifying ENTRESTO as the reference

listed drug. Novartis filed this lawsuit days later and sought a TRO and preliminary injunction.

On August 13, the District Court denied both requests but implemented a brief stay to permit Novartis to seek relief from this Court. This Court entered a stay pending appeal on August 19, concluding that Novartis "ha[d] satisfied the stringent requirements for a stay pending appeal." *See* Order (D.C. Cir. Aug. 19, 2024).

On October 13, the District Court granted the federal and intervenor-defendants' cross motions for summary judgment and denied Novartis's motion for summary judgment. Novartis appealed.

At the request of FDA and MSN, the Court lifted its stay in the first, preliminary-injunction appeal and dismissed that appeal. This Court also noted that Novartis had not moved for a stay in the appeal from the District Court's summary-judgment ruling. At the time, however, a separate administrative injunction put in place by the U.S. Court of Appeals for the Federal Circuit in patent litigation between Novartis and MSN precluded MSN from launching its product; there thus was no emergency, and no need for a belt-and-suspenders stay here.

On January 10, the Federal Circuit ruled in favor of Novartis and found the key patent in dispute to be valid. MSN had already admitted to infringement. But after issuing a decision on the merits, the Federal Circuit lifted its administrative injunction and denied Novartis's motion to continue it. Order, *Novartis Pharm.*

Corp. v. MSN Pharms., Inc., *et al.*, Nos. 2023-2218, 2023-2220, 2023-2221 (Fed. Cir. Jan. 10, 2025). Later that afternoon, the Delaware trial court overseeing the patent litigation restrained MSN from launching its product through **January 15, 2025**, when the patent expires. Because MSN now has threatened imminent launch of a product that should never have been approved in the first place, Novartis seeks emergency relief in this Court.

ARGUMENT

A request for a stay pending appeal requires the moving party to show it is likely to "prevail on the merits" of its request, the "prospect of irreparable injury" is substantial, there is comparatively little "possibility of harm" to the adverse parties, and the "public interest" favors maintaining the status quo. *Washington Metro. Area Transit Comm'n v. Holiday Tours, Inc.*, 559 F.2d 841, 843 (D.C. Cir. 1977); *Nken v. Holder*, 556 U.S. 418, 434 (2009). A motion for an administrative stay is governed by the same factors. D.C. Cir. R. 8(a)(1). Novartis readily satisfies each factor.

I. NOVARTIS IS LIKELY TO PREVAIL ON THE MERITS.

The District Court reached the merits of this case at summary judgment, ruling for the federal- and intervenor-defendants—but the merits continue to tilt sharply in favor of Novartis.

A. MSN's Labeling Impermissibly Carves Out Critical Safety Instructions.

Novartis's TITRATION study demonstrated that the modified dosing regimen results in fewer clinically relevant adverse events for a vulnerable patient group and allowed a greater proportion of these patients to reach the efficacious target dose. AR 3982–84; AR 3949. Upon reviewing the study, FDA observed that "[a] longer titration period with a starting dose of 50 mg bid may reduce the risk of hypotension, renal impairment and hyperkalemia in patients previously on a low dose of an [ACE inhibitor] or ARB," as well as patients who are not currently taking an ACE inhibitor or ARB. AR 301. The agency also stated that the TITRATION study's results "suggest[] that patients who were previously on low dose[s] of ACEi and ARBs might benefit from a slow up-titration regimen . . . rather than a fast up-titration regimen . . . ***We agree with the proposed titration strategy from a safety perspective.***" AR 311 (emphasis added).

The protected dosing regimen in Section 2.6 of ENTRESTO's labeling provides clear directions for patients and providers so that ENTRESTO is administered at a safe dose and on a tolerable schedule to a group of patients who may otherwise fail to achieve the target dose. AR 1471. This improved safety and tolerability allows patients who may previously have discontinued therapy to continue to benefit from ENTRESTO's proven effectiveness. Roop Decl. ¶ 8.

Now FDA wants to pull this back for MSN's product: While the modified dosing regimen may be beneficial to ACE/ARB-naïve patients, the agency asserts that the modified dosing language may be carved out of MSN's labeling because the dosing regime was not "necessary to Entresto®'s approval." ECF 63 at 11; ECF 52 at 26. That is not the standard. The agency's regulations governing labeling carve-outs require that the generic drug's labeling be no "*less* safe or effective than the listed drug for all remaining, non-protected conditions of use." 21 C.F.R. § 314.127(a)(7); 21 C.F.R. § 314.94(a)(8)(iv) (emphasis added). Novartis need not prove that the MSN labeling renders the product unsafe in all circumstances, nor must it prove that the dosing regimen was "necessary" to the drug's approval. Novartis need only show that the generic's labeling is *less* safe than ENTRESTO's, and Novartis made that showing. The agency ignored this standard, suggesting that the safety profile of the MSN generic need not match the safety profile of ENTRESTO.

FDA also posited that *other* sections of the MSN labeling are sufficient to overcome any safety issues because they explain how to treat a patient after an adverse event has occurred. That is exactly backwards from a safety perspective, and inconsistent with the agency's actions at the time it approved ENTRESTO's labeling. There is an obvious difference between *preventing* an adverse event from occurring (as in Section 2.6) and letting patients suffer a potentially preventable

adverse event and then advising on how to treat it after the fact (as in Section 5). And nothing in Section 5—or anywhere else in the label other than the language that will be excised—suggests to physicians that ACE/ARB-naïve patients would be at particular risk of these adverse events. Patients now may face the known risk of being administered MSN's product without the benefit of labeling FDA considered necessary for the safe use of ENTRESTO in patients.

The District Court found that FDA "provided a reasoned scientific basis" for its conclusion that the modified dosing carve-out would not render the MSN product less safe or effective. ECF 68 at 19. Even assuming that were true, it is the legal reasoning that is wrong. FDA acknowledged that the dosing regimen may reduce the risk of adverse reactions in the relevant patient population. AR 301. Yet to explain its approval of the carve-out, the agency stated that it is unknown whether the dosing regimen is the "safest" and "best-tolerated" option. AR 3949. Again, that misunderstands the regulatory standard: The question is whether the generic's labeling renders it *less* safe than the *listed drug*; if so, Novartis need not demonstrate that ENTRESTO's labeling is the *safest*.

FDA should not have approved the MSN product's labeling.

B. The MSN Product Does Not Have the Same Approved Indication as ENTRESTO.

The FDCA requires that a proposed generic product show that the "labeling proposed for the new drug is the same as the labeling approved for the listed drug."

21 U.S.C. § 355(j)(2)(A)(v). Generic labeling may differ from the labeling of the reference listed drug only if those differences are due to (as relevant here) the fact that different companies manufacture and distribute the products. And FDA can do that only, as relevant here, by *omitting* an indication or other aspect of labeling if needed.

FDA violated that requirement here. ENTRESTO is indicated for all patients with heart failure. AR 1470. For the MSN product, FDA did not omit an indication; instead it *rewrote* the approved indication to cover only patients with *reduced* ejection fraction, reverting to the now-superseded ENTRESTO labeling FDA approved back in 2015.

In doing so, the agency appears to ignore its own conclusion in 2021 that ENTRESTO's labeling should be changed to reflect essential new information regarding the safety and efficacy of ENTRESTO in treating an expanded set of patients. In revising the indication in 2021, FDA eliminated the previous reference to "reduced ejection fraction," and added two statements to the indication, both of which emphasize the importance of taking a patient's LVEF into consideration:

- "Benefits are most clearly evident in patients with left ventricular ejection fraction (LVEF) below normal," and
- "LVEF is a variable measure, so use clinical judgment in deciding whom to treat."

AR 1470.

But when describing the indicated patient population, FDA eschewed a quantitative measure of ejection fraction, to ensure that the drug could be used more broadly, for *all* heart failure patients. In approving the MSN labeling, FDA jettisoned that approach—which as it acknowledged below, reflected an updated understanding of heart failure—and reversed its own judgment. FDA's decision to rewrite the approved indication for generic products is unlawful, for several reasons.

1. The MSN Labeling Violates the FDCA by Reverting to a Superseded ENTRESTO Indication.

The statutory text is framed in the present condition: Both the statute and FDA's implementing regulations require sameness to "the labeling approved for the listed drug." 21 U.S.C. § 355(j)(2)(A)(v); 21 C.F.R. § 314.127(a)(7); 21 C.F.R. § 314.94(a)(8)(iv). "Same as the labeling approved for the listed drug" does not permit comparison between a generic drug's new labeling and a reference drug's old labeling: The MSN drug must be compared to what ENTRESTO's labeling says *now*. *See* AR 4579 (in assessing labeling carve-outs, the agency must "start with the currently approved labeling" and "earlier versions of the drug's labeling . . . have no relevance to this inquiry") (footnote omitted).

The MSN labeling blessed by the agency essentially reverts to the now-superseded indication for ENTRESTO by confining its use to the reduced ejection fraction population. But it is 2025, not 2015. A generic may *omit* an indication; it cannot rewind the clock and *rewrite* the indication as it once was.

2. The Generic Labeling Violates the FDCA and FDA's Regulations by Adding New Language.

The FDCA requires that the labeling for an approved generic be the "same" as the labeling for the reference listed product. 21 U.S.C. § 355(j)(2)(A). Under one limited exception to this principle, the ANDA labeling may differ from the labeling of the reference listed drug if those differences are due (as relevant here) to the fact that the products are "produced or distributed by different manufacturers." *Id.* § 355(j)(2)(A)(v). By operation of its plain text, the "different manufacturer" exception would permit differences in generic labeling to identify a different manufacturer, product name, or company address. For this reason, the agency's position violates the plain language of its governing statute.

By regulation, FDA has explained its views on the limited exceptions to the same-labeling requirement. FDA regulations provide that within the "different manufacturer" exception, the generic drug product may reflect a labeling carve-out to address marketing exclusivity granted by FDA or patent rights 21 C.F.R. §§ 314.127(a)(7), 314.94(a)(8)(iv). Only a specific type of revision is permitted: an "*omission of an indication* or other aspect of labeling protected by patent or accorded exclusivity under section 505(j)(5)(F)." *Id.* § 314.94(a)(8)(iv) (emphasis added).

The word "omission" has a clear meaning: It means to leave something out. *See, e.g.*, Merriam-Webster Dictionary (defining "omission" as "something left out"). Leaving out an approved indication is permissible; *rewriting* the indication is

not. When a drug has been approved for multiple indications and a generic is later approved for one of those indications, FDA takes the position that it may permit the generic manufacturer to market its product without the labeling for the reference listed drug's other indications. *See Bristol-Myers Squibb Co. v. Shalala*, 91 F.3d 1493, 1499–1500 (D.C. Cir. 1996). But when—as here—a reference drug's labeling has just one indication statement, FDA cannot allow a generic manufacturer to *rewrite* the portions of the single-indication labeling at will. No reasonable interpretation of the word "omission" permits the revision of language to modify the current indication to reflect something different.

The District Court resisted the premise, crediting the Government's assurances that FDA in fact compared the generic's labeling to ENTRESTO's current labeling. ECF 68 at 15. Setting aside whether it is mere coincidence that the MSN product's labeling matches ENTRESTO's original, superseded labeling rather than the extant version, the agency has still trapped itself in a vise: If FDA compared the generic's labeling to ENTRESTO's current labeling and yet still resurrected language from ENTRESTO's original labeling, the agency violated its governing statute.

C. The MSN Product Does Not Have the Same Active Ingredients as ENTRESTO.

Finally, FDA acted unlawfully in concluding that the MSN product satisfies the FDCA's active ingredient "sameness" test. FDA may approve only those generic

drug products that are pharmaceutically equivalent to their reference listed drug. That equivalence requires, among other things, that a generic share the "same" active ingredients as the listed drug. 21 U.S.C. § 355(j)(2)(A)(ii)(III).

In evaluating ENTRESTO, FDA stated that it is a complex formed from two separate drug substances, and it has identified those drug substances as sacubitril and valsartan. AR 1242. But the MSN product is comprised of sacubitril sodium and valsartan disodium—two separate salts. AR 1896. To get around this problem, the agency has now insisted that the active ingredient sameness test should be applied to these two salts, chemicals that are found in MSN's product, not ENTRESTO. AR 2784, 2800–01.

This is news to Novartis. In the decade-plus regulatory history of ENTRESTO, the active ingredients have never been identified as the separate sodium salts of sacubitril and valsartan. *E.g.*, AR 57–119, AR 801–934. These two separate salts are not identified in the NDA or in the ENTRESTO labeling, nor are they listed in the Orange Book. AR 57–119, AR 801–934, AR 1469–89. These separate salts do not occur at any stage in the manufacture, distribution, or administration of ENTRESTO. AR 801–934.

The District Court wrongly concluded that ENTRESTO and MSN's generic share the same active ingredients for "sameness" purposes by deferring to FDA's late-breaking revelation that both drug products contain separate "sacubitril sodium"

and "valsartan disodium." ECF 68 at 22. But that is circular at best. The court concluded FDA had "consistently" treated ENTRESTO as "a different solid state physical form of the same salts," *id.* at 24, but the portions of the administrative record the court cited reveal the opposite. The separate salt forms of the active ingredients are mentioned nowhere in the administrative record until MSN came along. The District Court thus wrongly deferred to FDA's sameness determination.

II. NOVARTIS WILL SUFFER IRREPARABLE HARM.

Market dynamics dictate that once MSN's product launches, it will be impossible for Novartis ever to regain the status quo. *See, e.g.*, *Endo Par Innovation Co., LLC v. Becerra*, No. 24-cv-999 (TJK), 2024 WL 2988904, at *8 (D.D.C. June 10, 2024) (finding irreparable harm from market entry). That harm will manifest in several different ways.

A. Loss Of Market Position

ENTRESTO is Novartis's best-selling drug product. Roop Decl. ¶¶ 6, 7. Once a purported generic version of ENTRESTO enters the market, pharmacists will not only have the option, but in some States, the *obligation*, to fill prescriptions written for either "ENTRESTO" or "sacubitril/valsartan" with the generic product, except in those rare cases when the physician expressly specifies the brand or the patient refuses to consent to substitution. *Id.* ¶ 17. Pharmacies are also incentivized

to fill the prescription with the generic product whenever possible, to maximize the pharmacy's reimbursement spread. *Id.* ¶ 18.

Because of these market dynamics, Novartis projects that ENTRESTO would experience a dramatic loss of sales in the weeks following generic entry. Roop Decl. ¶ 25 (estimating 28% loss of new-to-brand prescriptions within the first month of generic entry). These injuries cannot be undone: "Courts have recognized that price erosion and diminished sales can constitute irreparable harm." *Bayer HealthCare, LLC v. FDA*, 942 F. Supp. 2d 17, 26 (D.D.C. 2013). Nor, of course, can these losses be recouped from FDA. That a plaintiff is a large company at no risk of dissolution does not preclude emergency relief in such a situation. *See, e.g.*, *Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060, 1067 & n.6 (D.C. Cir. 1998); *Teva Pharms., USA, Inc. v. FDA & Torpharm*, 254 F.3d 316 (D.C. Cir. 2000). And for good reason: a large company may still suffer devastating losses on its best-selling product.

Unlawful entry of MSN's purported generic product will fundamentally and irretrievably affect the market. ENTRESTO occupies favorable positions on government and private payers' lists of approved prescription drugs, known as formularies. Roop Decl. ¶ 20. Upon entry of MSN's generic, Novartis expects that insurers would either drop ENTRESTO to a lower tier or remove it entirely. *Id.*

Once generic entry happens, even if the generic is later removed from the market, it will be next-to-impossible for Novartis to persuade insurers to voluntarily

move ENTRESTO back into a more favored position on formularies. *Id.* ¶¶ 22, 36. That will lead to ongoing (and irremediable) losses: First, it would make ENTRESTO unavailable to many patients, leaving them with access only to cheaper but vastly less effective treatments. *Id.* ¶ 13. That would especially be so because physicians tend to prescribe lower tier drugs and/or grant patients' requests for them—especially generic drugs, which are viewed to be interchangeable and cheap. *Id.* ¶ 21. And once third-party payers and pharmacy benefit managers see a lower generic price, they will extract price concessions from Novartis for ENTRESTO. Because those concessions also are contracted-for, even if MSN later exits the market, the concessions likely could not be reversed. *See id.* ¶ 36.

B. Reputational Harm and Loss of Goodwill

Without temporary relief, Novartis also will suffer reputational harm and an irretrievable loss of goodwill among patients, physicians, and others. *Id.* ¶¶ 34, 36. Injuries or side effects caused by purported generic ENTRESTO are likely to be unfairly attributed by physicians and patients to Novartis, and this is not a theoretical concern, given the generic's confusing labeling and missing dosage instructions. *Id.* ¶¶ 37, 38. As the manufacturer of the reference listed drug, Novartis will be forced to expend time and resources documenting, investigating, and responding to patient concerns that arise from substitution of a purported generic product—even when the issue originates with he generic product, not ENTRESTO. *Id.* ¶ 39. And after an

adverse experience with MSN's generic, patients, and prescribers are likely to reject *any* sacubitril/valsartan drug product, not revert back to ENTRESTO. *Id.* ¶ 32.

C. Research and Development

Because revenues from ENTRESTO are a critical part of Novartis's ability to develop new therapies that treat critical health conditions, *id.* ¶ 35, the "loss of research and development funding" as a result of a generic's market entry will be irreparable. *Bayer HealthCare*, 942 F. Supp. 2d at 26; *see* Roop Decl. ¶ 30 (detailing Novartis's plans to further expand into the cardiovascular health area). If an unlawfully approved generic enters the market, all of these important activities would be jeopardized. *Id.* ¶¶ 6, 10, 30. The resulting harms could not be remedied after the fact: Progress toward developing critical new therapies will stall, and Novartis will have been subjected to significant risk of falling behind its competitors. *Id.* ¶ 31

III. NO OTHER PARTIES WOULD BE HARMED BY A STAY.

There is no irreparable harm on the other side of the ledger. A short stay that preserves the status quo harms no one. FDA suffers no consequence if the stay were granted; it has no stake in the matter other than complying with the law. MSN has not launched its product. Temporary relief thus can "preserve the object of the controversy in its then existing condition—to preserve the status quo." *Aamer v. Obama*, 742 F.3d 1023, 1043 (D.C. Cir. 2014) (quotation omitted).

IV. A STAY WOULD PROTECT THE PUBLIC INTEREST.

"[T]here is a strong public interest in meticulous compliance with the law by public officials." *Fund for Animals, Inc. v. Espy*, 814 F. Supp. 142, 152 (D.D.C. 1993). A stay will benefit FDA by keeping it within the bounds of the law. It will benefit generic filers that stayed within statutory and regulatory bounds, creating an even playing field. And it will benefit the public by fulfilling the statutory scheme.

Patients will also suffer irreparable harm absent a stay. Physicians will mistakenly assume that ENTRESTO may not be prescribed for heart failure patients with preserved ejection fraction, and these patients will miss out on lifesaving therapies. *See* Roop Decl. ¶¶ 37, 38. If the dose modification information is omitted from purported generic versions of ENTRESTO, ACE/ARB-naïve patients will receive treatment according to the standard dosing recommendations and will be titrated up more quickly than is tolerable, jeopardizing their safety. *Id.* ¶ 16. And MSN's product will be prescribed to patients even though its approval impermissibly relied upon FDA's safety and effectiveness finding for ENTRESTO—a drug with a different active ingredient.

CONCLUSION

For the foregoing reasons, the Court should immediately extend an administrative stay to permit it the time required to consider Novartis's motion and any opposition and reply. The Court should then grant Novartis's emergency motion

and stay FDA's approval pending a decision on the merits. Novartis asks that an administrative stay be entered by 5PM on January 13, followed by a decision on Novartis's emergency stay motion by 5PM on January 15.

Respectfully submitted,

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Dated: January 12, 2025

Attorneys for Novartis Pharmaceuticals Corporation

CERTIFICATE OF COMPLIANCE

Pursuant to Fed. R. App. P. 32(g)(1), the undersigned hereby certifies that this document complies with the type-volume limitation of Fed. R. App. P. 27(d)(2).

1. Exclusive of the exempted portions of the document, as provided in Fed. R. App. P. 32(f), this document contains 4,825 words.

2. The document has been prepared in proportionally spaced typeface using Microsoft Word in 14-point Times New Roman font. As permitted by Fed. R. App. P. 32(g)(1), the undersigned has relied upon the word count feature of this word processing system in preparing this certificate.

/s/ Catherine E. Stetson
January 12, 2025 Catherine E. Stetson

CERTIFICATE OF SERVICE

I certify that on January 12, 2025, the foregoing was electronically filed through this Court's CM/ECF system, which will send a notice of filing to all registered users.

/s/ Catherine E. Stetson
Catherine E. Stetson